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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|------------------------------|------------------|
| 09/829,621 | 04/10/2001 | Moshe Flashner-Barak | 1662/52202 | 7987 |
| 26646 | 7590 | 07/30/2004 | EXAMINER | |
| KENYON & KENYON ONE BROADWAY NEW YORK, NY 10004 | | | CHANNAVAJALA, LAKSHMI SARADA | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1615 | |

DATE MAILED: 07/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/829,621

Applicant(s)

FLASHNER-BARAK, MOSHE

Examiner

Lakshmi S Channavajjala

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-22,24-29,32,33,35-52,54-59 and 62-71 is/are pending in the application.
- 4a) Of the above claim(s) 10,11,19,28,29 and 49 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-9, 12-18,20-22,24-29,32, 33,35-37,40-48,50-52,54-59 and 62-71 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

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DETAILED ACTION

Claims 1,3-9,12-18,20-22,24-29,32,33,35-37,40-48,50-52,54-59 and 62-71 have been examined.

The following outstanding rejection has been maintained:

Claims 1, 3-9, 12-18, 20-22, 24-29, 32, 33, 35-37, 40-48, 50-52, 54-59 and 62-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,277,391 to Seo et al in view of US 5,916,596 to Desai.

Double Patenting

Claims 33, 35, 43, 54, 55 and 62-71 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of US patent 6,569,459.

Response to Arguments

Applicant's arguments filed 2-9-04 have been fully considered but they are not persuasive.

35 USC 103(a):

Applicants argue that there is absolutely no teaching or suggestion in the prior art of local administration of a composition comprising a plurality of microparticles having at least one chemotherapeutic and a suspending solution of at least one apoptosis-inducing chemotherapeutic combined with an amount of a plasma protein effective in increasing the aqueous solubility of the apoptosis inducing chemotherapeutic in the suspending solution. Applicants argue that Desai is deficient in the teaching of liquid formulation containing microspheres incorporating chemotherapeutics. Further, applicants argue that Hegedus, like Desai, is deficient in teaching or

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suggesting a suspension of microspheres incorporating anti-tumor chemotherapeutic in a solution of the paclitaxel-plasma protein complex.

Applicants state that instant examples show the unexpected advantage attendant to local administration of the claimed composition, wherein the intratumoral injection of paclitaxel and HSA solution more effectively causes apoptosis more effectively throughout a larger percentage of the tumor volume, thus allowing better distribution of microspheres within the tumor.

Applicants also refer to example 2, where injection of paclitaxel and HSA solution reduced mammary tumor xenograft size as compared to taxol alone, a non-treatment group and a saline control.

Applicants arguments have been considered but not found persuasive because the prior art cited, Seo and Desai, together teach the claimed limitations i.e., microspheres containing chemotherapeutic in a suspending liquid, a combination of a plasma protein with chemotherapeutic compound, the former being a natural carrier for the chemotherapeutic compound. Instant claims are rejected based on obviousness and not anticipatory rejection.

Accordingly, it is not necessary that each and every reference of the combination cited teach all the limitations claimed. The motivation to include the plasma proteins in the chemotherapeutic composition i.e., microspheres suspension of Seo comes from the teaching of Desai, who suggests that plasma proteins are excellent and natural carriers for paclitaxel. Further, as it is implicit that a carrier substance naturally increases the availability of the substance for which it acts as a carrier. Thus, the plasma protein of Desai would have naturally increased the solubility and thus the availability of chemotherapeutic agent. Further, with respect to the increasing the solubility of the drug, examiner notes that instant claims are directed to a composition and not a

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method of increasing the solubility of a chemotherapeutic drug. The combination of the teachings of Seo and Desai et al provide the required motivation to arrive at the claimed composition comprising microparticles of chemotherapeutic and a plasma protein. With respect to applicants' unexpected results, it is examiners' position that, in view of the teachings of Desai, one of an ordinary skill in the art would have expected an increase in the solubility of paclitaxel by adding plasma proteins.

Double patenting rejection:

Applicants argue that application claims are neither species nor generic to the patent claims because the patented method of administering paclitaxel requires two steps of infusing paclitaxel, whereas instant claims only require local administration of a chemotherapeutic. However, applicants' arguments are not persuasive because irrespective of the type of administration, the obviousness is based on the composition. Instant claims are directed to a composition and the limitation "for local administration" is an intended use that has no patentable weight. Both instant and patented claims recite the combination of chemotherapeutic drug and plasma protein, for the same purposes i.e., to improve the solubility of the chemotherapeutic. The instant dosage form i.e., microspheres constitute a species of the generic "compositions comprising chemotherapeutic and plasma protein". While the patented claims do not state if the composition is in the form of microspheres, preparing a pharmaceutical dosage form in the form of microspheres or microparticles with an expectation to increase the solubility would have been obvious for a skilled artisan. Accordingly, instant claims are an obvious variant of the patented claims. Therefore, the double patenting rejection has been maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

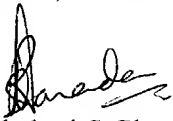
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Lakshmi S Channavajjala
Examiner
Art Unit 1615
July 28, 2004



Gollamudi S. Kishore, PhD
Primary Examiner
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For TR Page